PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P200301485WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/DK 03/00588	International filing date *(day/month/year)* 11.09.2003	Priority date *(day/month/year)* 11.09.2002
International Patent Classification (IPC) or both national classification and IPC C07H21/00		
Applicant SANTARIS PHARMA A/S et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
22.03.2004	26.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Klein, D Telephone No. +49 89 2399-7896

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/DK 03/00588

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-91 as originally filed

Claims, Numbers

1-28 as originally filed

Drawings, Sheets

1/11-11/11 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority in written form.

   ☒ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 10,19,20-25,27

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 10,19,20-25,27 are so unclear that no meaningful opinion could be formed *(specify)*:

   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-7, 12-17, 28
	No:	Claims	8,9,11,18,26,27
Inventive step (IS)	Yes:	Claims	1-7, 12-17, 28
	No:	Claims	8, 9, 11, 18,26,27
Industrial applicability (IA)	Yes:	Claims	1-25, 28
	No:	Claims	26-27

2. Citations and explanations

see separate sheet

Re Item III : No Opinion

a) Claim 10 is defined in terms of a functional definition and therefore does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The functional statement " ...wherein the ligand has a high affinity towards a receptor..." does not enable the skilled person to determine which technical feature is necessary to perform the stated function.

Furthermore, the relative term "..high affinity.." used in this same claim has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical feature to which it refer, thereby rendering the definition of the subject-matter of said claim unclear, Article 6 PCT.

b) The compound claim 19 refers to the use claim 20. Apparently, its dependance is wrong. Nevertheless, as it is not sure to which claim it refers, no examination will be carried out for claim 19.

c) Claims 20,23-25,27 are dependant on themselves. As it is not sure to which claim it refers, no examination will be carried out for these claims.

d) Claims 21-22 refer not only to compound claims but also to a use claim (claim 20). Therefore claims 21-22 are unclear, and no examination will be carried out for these claims.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:

D1: RAMIN HAMZAVI ET AL: "Modulation of the Pharmacokinetic Properties of PNA: Preparation of Galactosyl, Mannosyl, Fucosyl, N-Acetylgalactosaminyl, and N-Acetylglucosaminyl Derivatives of Aminoethylglycine Peptide Nucleic Acid Monomers and Their Incorporation into PNA Oligomers" BIOCONJUGATE CHEM., vol. 14, 2003, pages 941-954, XP002270930

D2: WO 98/53801 A (KNUDSEN HELLE ;NIELSEN PETER E (DK); ISIS PHARMACEUTICALS INC (US)) 3 December 1998 (1998-12-03)

The documents D3/D4 were not cited in the international search report. Copies of these documents are appended hereto.

D3 : Seitz et al. Chem Eur J. , 2001, vol 7, No 18, pp 3911-3925 : "Convergent Strategies for the attachment of fluorescing Reporter groups to Pepetide Nucleic Acids in Solution and on Solid phase".

D4 : Egholm et al. J. Am. Chem. Soc. , 1992,114, pp 1895-1897 : "Peptide Nucleic Acids (PNA). Oligonucleotide Analogues with an Achiral Peptide Backbone"

a) D1 which is an intermediate document published on 29/08/2003, is not prior art according to the Chap II PCT proceedings. Further, its content will not affect the novelty of the regional European proceeding to come.
Nevertheless, the extensive examination of that document, on the question whether it constitutes prior art or not, will depend essentially on the analysis of the claimed priority rights of the present application and will only be performed in the regional European proceedings to come.

b) The subject-matter of claims 1-7,12-17 concerns PNA mono- and oligomers derivatives bearing at least one "sugar" unit.

Since none of the available prior art discloses or suggests the subject-matter of claims 1-7, 12-17 these claims are considered new and inventive.

c) The subject-matter of claim 8 concerns an aeg-PNA (normal PNA) oligomer bound to one or more ligands.

Since there is not common accepted meaning of the term ligand, **any** substituent on an aeg-PNA is considered as a ligands (see D2-D4)

d) The documents D2-D4 disclose aeg-PNA molecules bearing modifications which are

considered as ligands, see for example D2 disclosing PNA bound to lipophilic substituents, D3 disclosing PNA bound to fluorescing reporter groups or D4 bearing a heteroaryl groups and Lys-NH_2 terminal groups.

Thus present claims 8,9,11,18,26,27 does not meet the criteria of novelty, Article 33(2) PCT.

Industrial Application Art. 33(4) PCT:

For the assessment of the present claims 26-27 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Clarity (Art. 6 PCT) :

The term "...and the like." employed in claims 20-21 is vague and unclear and leaves the reader in doubt as to what it refers therefore rendering the scope of said claims unclear. It should therefore be removed.